Combined EEG and MEG study of rolandic discharges in benign childhood epilepsy

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1 Introduction

Benign rolandic epilepsy of childhood (BREC) is one of the most frequent epileptic syndromes in children. Clinically the syndrome is characterized by facial motor seizures sometimes preceded by a somatosensory aura, speech arrest and by secondarily generalized tonic-clonic seizures during sleep. The prognosis is excellent and most patients become seizure-free by the age of 15 year [10, 11].

Interictal spikes show a stereotypical morphology with a negative sharp wave following by a positive wave, are located in the centro-temporal region, exhibit commonly a dipolar and relatively rarely a non-dipolar potential distribution and are activated by drowsiness and sleep stages III and IV [5, 8, 10, 13]. They have been studied extensively using advanced EEG data processing techniques including spike voltage topography as well as single and multiple dipole modeling [3-7, 9, 12]. These studies found that the interictal spike complex In BREC is generated either by single and multiple dipoles and that differences in spike characteristics exist between patients with typical and atypical BREC.

Nevertheless the neurogenesis of the interictal spike complex in BREC still remains controversial. Magnetoencephalography (MEG) may be helpful to clarify some of these questions because it provides both complementary and confirmatory information to the scalp-EEG. However only few MEG studies in BREC have been reported so far [1, 2, 4, 15]: no simultaneous MEG and EEG studies using modern whole-head MEG systems and large number of EEG channels have been reported.

We therefore performed a combined neuroelectric and neuromagnetic study in 24 patients with BREC using a 143 channel whole-head MEG system simultaneously with EEG recorded from closely spaced scalp-EEG electrodes.

2 Methods

2.1 Patient studies

We investigated 24 consecutive patients with benign rolandic epilepsy of childhood (BREC) (12 boys and 12 girls, age 6 – 14 years, mean 10.8 years, median 11 years, age at onset of disease 3.5-12.3 years, mean 5.2 years), diagnosed on the basis of a typical history, seizure semiology reported by the patients and/or their parents, typical interictal spikes on routine EEG and a normal MRI-scan.

Three patients showed mild to moderate developmental delay as assessed by formal neuropsychological testing, so they were classified as atypical BREC [5]. Informed written consent to participate in the EEG/MEG study was obtained from the parents of all patients.

2.2 MEG and EEG recordings

We performed 2-3 hour recording sessions of simultaneous scalp-EEG and MEG. Neuromagnetic recordings were performed with a whole-head 143 channel MEG system (CTF Systems Inc., Port Coquitlam, B.C. Canada) in a large magnetically shielded room (Vacuumschmelze GmbH, Hanau, Germany). Scalp-EEG was recorded simultaneously from 40 gold-disk electrodes placed according to the extended International 10-20 System using Pz as reference electrode. Data were collected from manually triggered epochs of 5 s duration. EEG and MEG signals were amplified, filtered (bandpass 1-70 Hz), analog-to-digital converted (sampling frequency = 250 Hz) and stored digitally for off-line data analysis. Only spikes during wakefulness were analyzed, because they are generally considered to be of higher localizing significance [14].

Rolandic discharges were manually selected from raw EEG/MEG data. At least 10 spikes consisting of a prominent negative sharp wave and a following positive wave were extracted from the EEG/MEG recordings for each patient. In order to avoid artificial time delays by averaging variable spike populations we exclusively used spontaneous spikes for analysis. Data analysis was performed on a time window from 500 ms before to 500 ms after the peak of the most prominent negative peak of the sharp wave.

First, isopotential and isofield maps were calculated using spherical spline interpolation at 4 msec time intervals. Second, spikes were subjected to a dipole source analysis using the BESA software (Megis, Munich, Germany) for the EEG data and the CTF Systems software for the MEG data. We performed principal component analysis (PCA) and spatio-temporal dipole modeling on EEG data in order to estimate the number of active sources. We used EEG for this type of analysis because EEG provides more complete information and both tangential and radial sources can be detected. If PCA and spatio-temporal dipole modeling indicated only one significant source generating the interictal spike complex, we used single equivalent current dipole (ECD) modeling for both MEG and EEG data during the subsequent analysis.

3 Results

During the combined EEG/MEG recordings we could not record spikes in 4 patients (16.7 %) and another 3 patients (12.5%) had to be excluded from further analysis because of movement artifacts precluding a meaningful data analysis. Thus data from 17 patients (70.8%) were included in the final analysis.

The EEG/MEG recordings showed right-sided spikes in 6 patients (35%), left-sided spikes in 9 patients (53%) and independent bilateral centrotemporal epileptiform abnormalities in 2 patients (12%).

3.1 EEG recordings

On scalp-EEG spikes showed a similar morphology both within and across patients. Specifically the 3 patients with atypical BREC could not be distinguished from typical BREC patients based on spike configuration. All spikes were characterized by a stabile dipolar potential distribution over the entire time domain with a negativity located over the centro-temporal region and frontal positivity (Fig.1a). PCA revealed one significant component underlying the interictal spike complex. Spatio-temporal dipole modeling as well indicated one source, adding additional sources did not significantly increase the variance accounted for by the model. We therefore used an instantaneous single dipole model for further analysis. The dipoles showed a stable location and orientation over the entire time epoch analyzed (Fig. 1b).

Dipole location and orientation were of similar stability in patients with atypical BREC as compared to patients with typical BREC. All sources were located in the central region and oriented tangentially to the cortical surface with a frontal positivity and a centro-temporal negativity which showed a phase reversal that corresponded approximately to central sulcus.

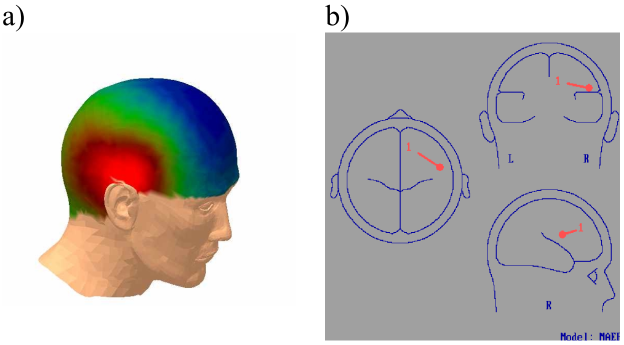

Figure 1: *EEG recordings: a) stabile dipolar potential distribution with a negativity located over the centro-temporal region and frontal positivity. b) instantaneous single dipole, which showed a stable location and orientation over the analyzed time epoch.*

3.2 MEG recordings

Similar to the findings on EEG, MEG spikes were characterized by a stereotypical appearance both within and across patients. The magnetic field distribution showed a stable dipolar field with magnetic flux exiting from the head over the parietal region and magnetic flux reentering the head anterior temporal (Fig. 2).

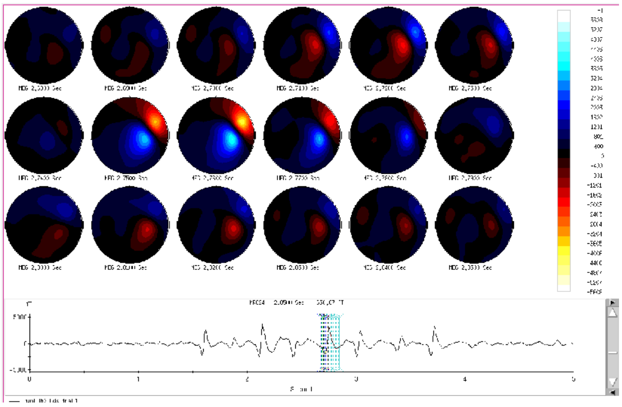

Figure 2: *MEG recordings: magnetic field distribution which showed stable dipolar field with magnetic flux exiting from the head over the parietal region (blue) and magnetic flux reentering the head anterior temporal (red).*

On single dipole modeling the estimated dipolar sources were located in the central region with the positive pole pointing frontally (Fig. 3). No differences in spike location, orientation and stability of both location or orientation were found between patients with typical and atypical BREC.

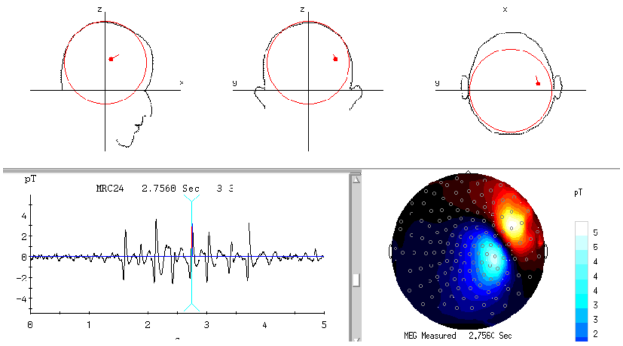

Figure 3: *MEG recordings: instantaneous single dipole, which showed a stable location and orientation over the analyzed time.*

The rolandic discharges of two patients with bilateral spikes showed similar patterns of magnetic field distribution, dipole locations and orientations as compared with the patients with unilateral spikes.

3.3 Comparison of EEG and MEG results:

Applying simultaneous EEG and MEG in patients with BREC, we could find that spikes were characterized by similarity according to field distribution in all patients. One source with centro-temporal negativity and frontal directed positivity was enough to explain the data at the peak of the spike amplitude. The direction between the field maxima of EEG and MEG was orthogonal to each other.

4 Discussion

Our results indicate that the interictal spike complex in most patients with BREC is generated by a single tangential dipolar source in the central region. Both EEG and MEG showed a stable dipolar field distribution over the a time window from 250 msec before to 250 msec after the maximum of the negative peak of the interictal spike complex. Because MEG and EEG yield both complementary and confirmatory information the finding of a single source with both modalities further confirms this hypothesis of a single source. Because EEG is sensitive towards both tangential and radial sources, we investigated the possible existence of an additional radial source using PCA and multiple dipole modeling applied to the EEG data. However, even with this approach no such source could be detected. In a previous EEG study from our group we found interictal spike complexes generated by single and multiple dipoles in an about equal number of patients with BREC. This discrepancy can possibly be explained by a more homogenous patient population investigated in the present study.

We could not find differences in dipole location, orientation and stability over time between our patients with typical and atypical BREC. This is in contrast to previous reports on EEG recordings in patients with BREC. Wong and colleagues [5, 12] suggested that typical patients were characterized by dipolar field distributions whereas atypical patients frequently exhibited non-dipolar epileptiform discharges. Wong [6] found that in typical BREC the source locations clustered more tightly around the central sulcus as compared with atypical cases. Finally, Weinberg at al. [7] suggested that single dipole fits may be more predictive of typical BREC than multiple dipole fits. We believe that the number of patients in our study is certainly too small to draw definite conclusions on a differentiation of typical and atypical BREC based on the configuration of the interictal spike complex.

In conclusion combined EEG and MEG dipole modeling are useful to better understand the pathophysiology of the interictal spike complex in BREC.

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